REMARKS

Applicants thank the Examiner for the thorough examination given the present application.

Status of the Claims

Claims 1-8 are pending in the present application. Claims 6-8 are currently withdrawn from consideration. Claim 1-5 have been amended. Support for the recitation of "solid composition" in the amended claims can be found in the present specification, *inter alia*, at page 10, lines 23-26. No new matter has been added by way of the above amendment. Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Examiner's Interview

Applicants would like to thank the Examiner for his time during the interview on February 25, 2009. Applicants appreciate the courtesies extended to them in this application. In compliance with MPEP 713.04, Applicants submit the following remarks.

The Interview Summary sufficiently summarizes the discussions during the interview. Although an agreement could not be reached, Applicants believe that the claims are now in condition for allowance. Should the Examiner believe that there remains any outstanding issues, Applicants respectfully request that the Examiner contact Applicants' Representative so as to expedite resolution of these outstanding issues, via an Examiner's Amendment or the like.

Issues under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-5 under 35 U.S.C. § 103(a) as being unpatentable over Suzuki et al. '730 (US 7,244,730) in view of FDA Drug Application No. NDA #019437. Applicants respectfully traverse, and reconsideration and withdrawal of this rejection are respectfully requested.

Legal Standard for Determining Prima Facie Obviousness

MPEP 2141 sets forth the guidelines in determining obviousness. First, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), which has provided the controlling framework for an obviousness analysis. The four *Graham* factors are:

(a) determining the scope and content of the prior art;

(b) ascertaining the differences between the prior art and the claims in issue;

(c) resolving the level of ordinary skill in the pertinent art; and

(d) evaluating any evidence of secondary considerations.

Graham v. John Deere, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966).

Second, the Examiner has to provide some rationale for determining obviousness. MPEP 2143 sets forth some rationales that were established in the recent decision of *KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). Exemplary rationales that may support a conclusion of obviousness include:

(a) combining prior art elements according to known methods to yield predictable results;

(b) simple substitution of one known element for another to obtain predictable results;

(c) use of known technique to improve similar devices (methods, or products) in the same way;

(d) applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;

(e) "obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success

(f) known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;

(g) some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

As the MPEP directs, all claim limitations must be considered in view of the cited prior art in order to establish a *prima facie* case of obviousness. *See* MPEP 2143.03.

Distinctions over the Cited Art

As amended, independent claims 1 and 3 are directed to a "***solid*** composition."

In stark contrast, Suzuki et al. '730 and FDA Drug Application No. NDA #019437 merely disclose an oral or injectable composition, which is understood to have a liquid form. During the interview, the Examiner indicated that the drug of FDA Drug Application No. NDA #019437 may be in solid form. However, enclosed herewith is a copy of the drug information regarding Aminosyn II, which has been obtained from the website of HOSPIRA, Inc., the seller of the products in FDA Drug Application No. NDA #019437. This drug information shows that the drug in FDA Drug Application No. NDA #019437 is a sterile, nonpyrogenic **solution** for intravenous infusion (see DESCRIPTION section on page 1). Therefore, the drug in FDA Drug Application No. NDA #019437 is a liquid composition.

To establish a *prima facie* case of obviousness of a claimed invention, all of the claim limitations must be disclosed by the cited references. As discussed above, the cited references fail to disclose all of the claim limitations of independent claims 1 and 3, and those claims dependent thereon. Accordingly, the combination of references does not render the present invention obvious. Furthermore, the cited references or the knowledge in the art provide no reason or rationale that would allow one of ordinary skill in the art to arrive at the present invention as claimed. Therefore, a *prima facie* case of obviousness has not been established, and withdrawal of the outstanding rejection is respectfully requested. Any contentions of the USPTO to the contrary must be reconsidered at present.

Obviousness-Type Double Patenting

Claims 1-5 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13 and 14 of U.S. Patent No. 7,244,730 (Suzuki et al. '730).

Applicants respectfully submit that the double patenting rejection has been overcome for the reasons given above regarding Suzuki et al. '730. Thus, withdrawal of the outstanding rejection is respectfully requested.

CONCLUSION

A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case clearly indicating that each of claims 1-5 are allowed and patentable under the provisions of title 35 of the United States Code.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Chad M. Rink, Reg. No. 58,258 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: MAR 2 6 2009

Respectfully submitted,

By _____
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Attachment: copy of the drug information regarding Aminosyn II

Aminosyn® II 3.5% M and 4.25% M
in Dextrose Injection

℞ only

AN AMINO ACID INJECTION WITH MAINTENANCE ELECTROLYTES IN DEXTROSE INJECTION

NOTE: These solutions are hypertonic. See WARNINGS and PRECAUTIONS.

Nutrimix® Dual-chamber Flexible Container

The Upper Chamber Contains 500 mL of Aminosyn II with Maintenance Electrolytes (An Amino Acid Injection with Maintenance Electrolytes)

The Lower Chamber Contains 500 mL of Dextrose Injection, USP

DESCRIPTION

Upper Chamber: Contains 500 mL of Aminosyn II 3.5% M or 4.25% M (an amino acid injection with maintenance electrolytes) — a sterile, nonpyrogenic solution for intravenous infusion. Formulations are described below.

Lower Chamber: Contains 500 mL of Dextrose Injection, USP — a sterile, nonpyrogenic, hypertonic solution of Dextrose, USP in water for injection. The table below indicates the characteristics of this concentrated solution.

The container must be used only after removing the clamp and thoroughly mixing the contents of the two chambers. Mixing the contents of the upper and lower chambers yields a concentrated source of amino acids and carbohydrate calories for intravenous infusion. Headspace contains Nitrogen gas.

UPPER CHAMBER COMPOSITION (500 mL)

Essential Amino Acids (mg/100 mL)

Aminosyn II	7% M*	8.5% M*
Isoleucine	462	561
Leucine	700	850
Lysine (acetate)**	735	893
Methionine	120	146
Phenylalanine	209	253
Threonine	280	340
Tryptophan	140	170
Valine	350	425

*Contains maintenance electrolytes.
**Amount cited is for lysine alone and does not include the acetate salt.

Nonessential Amino Acids (mg/100 mL)

Aminosyn II	7% M*	8.5% M*
Alanine	695	844
Arginine	713	865
Aspartic Acid	490	595
Glutamic Acid	517	627
Glycine	350	425
Histidine	210	255
Proline	505	614
Serine	371	450
N-Acetyl-L-Tyrosine	189	230

*Contains maintenance electrolytes.

Hospira, Inc., Lake Forest, IL 60045 USA Reference EN-0130

Aminosyn® II 3.5% M and 4.25% M
in Dextrose Injection

Electrolytes (mEq/L) [a]

Aminosyn II	7% M	8.5% M
Sodium [b] (Na^+)	82	87.4
Potassium (K^+)	26	26
Chloride (Cl^-)	73	73
Magnesium (Mg^{++})	6	6
Phosphorus [c] (P)	7 (mM)	7 (mM)
Acetate [d] ($C_2H_3O^-_2$)	50.2	61
Sodium Hydrosulfite added (mg/100 mL)	60	60
Osmolarity (actual mOsmol/L)	719	811
pH	5.8	5.8
range [e]	5.0 — 6.5	5.0 — 6.5

[a] Electrolyte concentrations cited in mEq/L must be divided by two in order to derive the amounts present in the 500 mL upper chamber.
[b] Includes sodium from the pH adjustor, sodium hydroxide, and from the antioxidant, sodium hydrosulfite.
[c] mM = millimoles; one mM of phosphorus = 31 mg phosphorus.
[d] From lysine acetate.
[e] Contains sodium hydroxide for pH adjustment.

LOWER CHAMBER COMPOSITION (500 mL)

Dextrose Injection, USP	10% Dextrose	20% Dextrose
Dextrose, hydrous (g/500 mL)	50	100
Energy (kcal/500 mL)	170	340
Osmolarity (actual mOsmol/L)	546	934
pH	4.3	4.3
range	3.2 — 6.5	3.2 — 6.5

COMBINED ADMIXTURE COMPOSITION (1000 mL)

Essential Amino Acids (mg/100 mL)

Aminosyn II	3.5% M*	4.25% M*
Isoleucine	231	280
Leucine	350	425
Lysine (acetate)**	368	446
Methionine	60	73
Phenylalanine	104	126
Threonine	140	170
Tryptophan	70	85
Valine	175	212

*Contains maintenance electrolytes.
**Amount cited is for lysine alone and does not include the acetate salt.

Hospira, Inc., Lake Forest, IL 60045 USA Reference EN-0130

Aminosyn® II 3.5% M and 4.25% M
in Dextrose Injection

Nonessential Amino Acids (mg/100 mL)

Aminosyn II	3.5% M*	4.25% M*
Alanine	348	422
Arginine	356	432
Aspartic Acid	245	298
Glutamic Acid	258	314
Glycine	175	212
Histidine	105	128
Proline	252	307
Serine	186	225
N-Acetyl-L-Tyrosine	94	115

*Contains maintenance electrolytes.

Electrolytes (mEq/L)

Aminosyn II	3.5% M* in D5-W	4.25% M* in D10-W
Sodium [a] (Na^+)	41	43.7
Potassium (K^+)	13	13
Chloride (Cl^-)	36.5	36.5
Magnesium (Mg^{++})	3	3
Phosphorus [b] (P)	3.5 (mM)	3.5 (mM)
Acetate [c] ($C_2H_3O^-_2$)	25.1	30.5
Sodium Hydrosulfite added (mg/100 mL)	30	30
Osmolarity (actual mOsmol/L)	616	919
pH	5.8	5.8
range [d]	5.0 — 6.5	5.0 — 6.5
Total Amino Acids (g/L)	35	42.5
Protein Equivalent (g/L)	35	42.5
Total Nitrogen (g/L)	5.35	6.5

* Contains maintenance electrolytes.
[a] Includes sodium from the pH adjustor, sodium hydroxide, and from the antioxidant, sodium hydrosulfite.
[b] mM = millimoles; one mM of phosphorus = 31 mg phosphorus.
[c] From lysine acetate.
[d] pH adjusted with sodium hydroxide.

After admixture, the formulation contains the following added ingredients per 100 mL:
Aminosyn II 3.5% M in 5% Dextrose Injection
Aminosyn II 4.25% M in 10% Dextrose Injection

Sodium chloride, 120 mg; potassium chloride, 97 mg; magnesium chloride (hexahydrate), 30 mg; dibasic sodium phosphate (anhydrous), 49.3 mg; and sodium hydrosulfite added, 30 mg.

Sodium Chloride, USP is chemically designated NaCl, a white crystalline compound freely soluble in water.

Potassium Chloride, USP is chemically designated KCl, a white granular powder freely soluble in water.

Magnesium Chloride, USP (hexahydrate) is chemically designated $MgCl_2 \cdot {}_6H_2O$, deliquescent crystals very soluble in water.

Dibasic Potassium Phosphate, USP (anhydrous) is chemically designated K_2HPO_4, white granules very soluble in water.

Dibasic Sodium Phosphate, USP (anhydrous) is chemically designated Na_2HPO_4, colorless or white granular salt freely soluble in water.

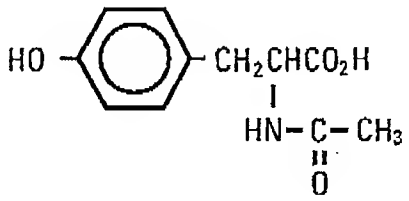
Hospira, Inc., Lake Forest, IL 60045 USA Reference EN-0130

Aminosyn® II 3.5% M and 4.25% M
in Dextrose Injection

Dextrose, USP is chemically designated D-glucose, monohydrate ($C_6H_{12}O_6 \cdot H_2O$), a hexose sugar freely soluble in water.

The formulas for the individual amino acids are as follows:

Essential Amino Acids	
Isoleucine, USP	$C_6H_{13}NO_2$
Leucine, USP	$C_6H_{13}NO_2$
Lysine Acetate, USP	$C_6H_{14}N_2O_2 \cdot CH_3COOH$
Methionine, USP	$C_5H_{11}NO_2S$
Phenylalanine, USP	$C_9H_{11}NO_2$
Threonine, USP	$C_4H_9NO_3$
Tryptophan, USP	$C_{11}H_{12}N_2O_2$
Valine, USP	$C_5H_{11}NO_2$
Nonessential Amino Acids	
Alanine, USP	$C_3H_7NO_2$
Arginine, USP	$C_6H_{14}N_4O_2$
Aspartic Acid	$C_4H_7NO_4$
	$HO_2CCH_2CH(NH_2)CO_2H$
Glutamic Acid	$C_5H_9NO_4$
	$HO_2CCH_2CH_2CH(NH_2)CO_2H$
Glycine, USP	$C_2H_5NO_2$
Histidine, USP	$C_6H_9N_3O_2$
Proline, USP	$C_5H_9NO_2$
Serine, USP	C_3H7NO_3
N-Acetyl-L-Tyrosine	$C_{11}H_{13}NO_4$



The flexible plastic container is fabricated from a specially formulated nonplasticized thermoplastic co-polyester (CR3). Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly. Solutions inside the plastic container also can leach out certain of its chemical components in very small amounts before the expiration period is attained. However, the safety of the plastic has been confirmed by tests in animals according to USP biological standards for plastic containers.

CLINICAL PHARMACOLOGY

Aminosyn II 3.5% M or 4.25% M in Dextrose Injection obtained upon mixing thoroughly the contents of the two chambers, provides carbohydrate calories and crystalline amino acids to stimulate protein synthesis, to limit protein catabolism, to minimize liver glycogen depletion and to promote wound healing. The infusion of this mixture through a central or peripheral venous line should be considered to approximate the protein and calorie requirements for patients receiving total parenteral nutrition. I.V. lipids may be infused simultaneously to provide adequate calories, if desired.

Aminosyn® II 3.5% M and 4.25% M
in Dextrose Injection

INDICATIONS AND USAGE

Aminosyn II 3.5% M or 4.25% M in Dextrose Injection is indicated for intravenous infusion in the prevention of nitrogen loss and negative nitrogen balance in cases where (a) the gastrointestinal tract by the oral, gastrostomy or jejunostomy route cannot or should not be used, (b) gastrointestinal absorption of nutrients is impaired or (c) metabolic requirements for protein and calories are substantially increased as with extensive burns and (d) morbidity and mortality may be reduced by replacing amino acids lost from tissue breakdown, thereby preserving tissue reserves, as in acute renal failure. In such patients intravenous feeding for more than a few days would be expected.

The addition of supplemental electrolytes such as trace metal additives, or multivitamin additives will be in accordance with the prescription of the attending physician.

CONTRAINDICATIONS

This preparation should not be used in patients with hepatic coma or metabolic disorders involving impaired nitrogen utilization.

WARNINGS

Aminosyn II 4.25% M in 10% Dextrose Injection is hypertonic, but it may be delivered by peripheral vein only if lipid emulsion is administered simultaneously.

Intravenous infusion of amino acids may induce a rise in blood urea nitrogen (BUN), especially in patients with impaired hepatic or renal function. Appropriate laboratory tests should be performed periodically and infusion discontinued if BUN levels exceed normal postprandial limits and continue to rise. It should be noted that a modest rise in BUN normally occurs as a result of increased protein intake.

Administration of amino acid solutions to a patient with hepatic insufficiency may result in serum amino acid imbalances, metabolic alkalosis, prerenal azotemia, hyperammonemia, stupor and coma.

Administration of amino acid solutions in the presence of impaired renal function may augment an increasing BUN, as does any protein dietary component.

Solutions containing sodium ion should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency and in clinical states in which there exists edema with sodium retention.

Solutions containing potassium ions should be used with great care, if at all, in patients with hyperkalemia, severe renal failure and in conditions in which potassium retention is present.

Solutions containing acetate ion should be used with great care in patients with metabolic or respiratory alkalosis. Acetate should be administered with great care in those conditions in which there is an increased level or an impaired utilization of this ion, such as severe hepatic insufficiency.

Solutions of Aminosyn II 3.5% M or 4.25% M in Dextrose Injection contain sodium hydrosulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

(Admixtures of Aminosyn II 3.5% M or 4.25% M in Dextrose Injection with an amino acid concentration greater than 2.5% are too concentrated for administration to infants.)

Instances of asymptomatic hyperammonemia have been reported in patients without overt liver dysfunction. The mechanisms of this reaction are not clearly defined, but may involve genetic defects and immature or subclinically impaired liver function.

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who

receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

Special care must be taken when administering glucose to diabetic or prediabetic patients. To control and minimize hyperglycemia and consequent glycosuria, it is desirable to monitor blood and urine glucose and, if necessary, add insulin.

Because of its antianabolic activity, concurrent administration of tetracycline may reduce the nitrogen sparing effects of infused amino acids.

Intravenously administered amino acids should be used with caution in patients with history of renal disease, pulmonary disease, or with cardiac insufficiency so as to avoid excessive fluid accumulation.

Nitrogen intake should be carefully monitored in patients with impaired renal function.

SPECIAL PRECAUTIONS FOR CENTRAL INFUSIONS
ADMINISTRATION BY CENTRAL VENOUS CATHETER SHOULD BE USED ONLY BY THOSE FAMILIAR WITH THIS TECHNIQUE AND ITS COMPLICATIONS

Central vein infusion of nutrient solutions requires a knowledge of nutrition as well as clinical expertise in recognition and treatment of complications. Attention must be given to solution preparation, administration and patient monitoring. IT IS ESSENTIAL THAT A CAREFULLY PREPARED PROTOCOL BASED ON CURRENT MEDICAL PRACTICES BE FOLLOWED, PREFERABLY BY AN EXPERIENCED TEAM.

SUMMARY HIGHLIGHTS OF COMPLICATIONS
(See also Current Medical Literature).

1. **Technical:**
   The placement of a central venous catheter should be regarded as a surgical procedure. One should be fully acquainted with various techniques of catheter insertion. For details of technique and placement sites, consult the medical literature. X-ray is the best means of verifying catheter placement. Complications known to occur from the placement of central venous catheters are pneumothorax, hemothorax, hydrothorax, artery puncture and transection, injury to the brachial plexus, malposition of the catheter, formation of arteriovenous fistula, phlebitis, thrombosis and air and catheter emboli.
2. **Septic:**
   The constant risk of sepsis is present during administration of total parenteral nutrition. It is imperative that the preparation of the solution and the placement and care of catheters be accomplished under strict aseptic conditions.

   Solutions should be used promptly after mixing. Storage should be under refrigeration and limited to a brief period of time, preferably less than 24 hours.

   Administration time for a single container and set should never exceed 24 hours.
3. **Metabolic:**
   The following metabolic complications have been reported: metabolic acidosis and alkalosis, hypophosphatemia, hypocalcemia, osteoporosis, hyperglycemia, hyperosmolar nonketotic states and dehydration, glycosuria, rebound hypoglycemia, osmotic diuresis and dehydration, elevated liver enzymes, hypo- and hypervitaminosis, electrolyte imbalances and hyperammonemia in children. Frequent evaluations are necessary especially during the first few days of therapy to prevent or minimize these complications.

   Administration of glucose at a rate exceeding the patient's utilization rate may lead to hyperglycemia, coma and death.

Pregnancy Category C. Animal reproduction studies have not been conducted with Aminosyn II with maintenance electrolytes in dextrose injection. It is not known whether this admixture can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Aminosyn II 3.5% M or 4.25% M in Dextrose Injection should be given to pregnant women only if clearly needed.

Pediatric Usage
Due to their concentration, these solutions are not recommended for use in pediatric patients less than 1 year old. Frequent monitoring of serum glucose concentrations is required when dextrose is prescribed to pediatric patients, particularly neonates and low birth weight infants.

Geriatric Use
Clinical Studies of Aminosyn II 3.5% M or 4.25% M in Dextrose Injection have not been performed to determine whether patients over 65 years of age respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. This drug is known to be substantially excreted by kidney, and the risk for adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

CLINICAL EVALUATION AND LABORATORY DETERMINATIONS, AT THE DISCRETION OF THE ATTENDING PHYSICIAN, ARE NECESSARY FOR PROPER MONITORING DURING ADMINISTRATION. Do not withdraw venous blood for blood chemistries through the infusion site, as interference with estimations of nitrogen-containing substances may occur. Blood studies should include glucose, urea nitrogen, serum electrolytes, ammonia, cholesterol, acid-base balance, serum proteins, kidney and liver function tests, osmolarity and hemogram. White blood count and blood cultures are to be determined if indicated. Urinary osmolality and glucose should be determined as necessary.

Do not use unless the solutions are clear and container is undamaged. Discard unused portion.

Do not use if solution in either chamber is discolored or if clamp is open or missing.

This product contains no more than 25 mcg/L of aluminum.

ADVERSE REACTIONS
Hyperosmolar syndrome, resulting from excessively rapid administration of concentrated dextrose may cause mental confusion and/or loss of consciousness.

Reactions which may occur because of the solution or the technique of administration include febrile response, infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection, extravasation and hypervolemia.

Generalized flushing, fever and nausea also have been reported during peripheral infusions of amino acid solutions.

If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of the fluid for examination if deemed necessary.

OVERDOSAGE
In the event of overhydration or solute overload, re-evaluate the patient and institute appropriate corrective measures. See WARNINGS and PRECAUTIONS.

DOSAGE AND ADMINISTRATION
The total daily dose of Aminosyn II 3.5% M or 4.25% M in Dextrose Injection to be infused depends on daily protein and caloric requirements and on the patient's metabolic and clinical response. In many patients, provision of adequate calories in the form of dextrose may require the administration of exogenous insulin to prevent hyperglycemia and glycosuria. To prevent rebound hypoglycemia, a solution containing

5% dextrose should be administered when hypertonic dextrose infusions are abruptly discontinued.

As reported in the literature, the dosage and constant infusion rate of intravenous dextrose must be selected with caution in pediatric patients, particularly neonates and low birth weight infants, because of the increased risk of hyperglycemia/hypoglycemia.

As with all intravenous fluid therapy, the parenteral administration of a solution of amino acids and dextrose requires an accurate estimate of the total fluid and electrolytes needed to compensate for the patient's measurable urinary and other (i.e., nasogastric suction, fistula drainage, diarrhea) daily losses. After estimating the total daily fluid (water) requirements, the appropriate volume to be infused to meet the daily protein requirement of the patient can be determined. The balance of fluid needed beyond the volume of the amino acid/dextrose solution can be provided by other solutions suitable for intravenous infusion. I.V. lipid emulsions may also be infused to deliver additional calories if required. Lipid emulsion can be administered to provide up to 3 g fat/kg/day, infused simultaneously with Aminosyn II 3.5% M or 4.25% M in Dextrose Injection by means of a Y-connector located near the infusion site, using separate flow controls for each solution. Aminosyn II 3.5% M or 4.25% M in Dextrose Injection may be premixed with fat emulsion, but only in the 2000 mL Nutrimix II container. Vitamins and trace minerals may be added to the amino acid/dextrose solution as needed.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

The total daily dose of the amino acid/dextrose solution to be infused depends on daily protein requirements and on the patient's metabolic and clinical response. The daily determination of nitrogen balance and accurate body weights, corrected for fluid balance, are probably the best means of assessing individual protein requirements.

Adult Patients

The daily nutrient requirements of an average adult patient, not hypermetabolic, in an acceptable weight range and with restricted physical activity, are about 30 kcal/kg of body weight, 12 to 18 grams of nitrogen (or 1.0 to 1.5 g amino acids/kg/day) and between 2500 and 3000 mL of fluids. In depleted and severely traumatized patients such as burned patients or patients who have received major surgery with complications, the requirements for nutrients and fluids may be significantly higher. In such cases, 4000 calories and 25 grams of nitrogen or more may be required daily to achieve nitrogen balance. The fluid losses through drainages and wound surface must be taken into account in calculating the fluid requirements of these patients.

Fat emulsion administration should be considered when prolonged parenteral nutrition is required in order to prevent essential fatty acid deficiency (EFAD). Serum lipids should be monitored for evidence of EFAD in patients maintained on fat-free TPN.

The infusion rate for central vein admixtures of Aminosyn II 4.25% M in Dextrose Injection should be 2 mL/min initially and may be gradually increased to deliver the required amounts of amino acids and calories. If nutrient administration falls behind schedule, under no circumstances should an attempt to "catch up" to planned intake be made. The rate of nutrient infusion is governed by the protein requirements and by the patient's glucose tolerance estimated by glucose levels in plasma and urine. The maximum rate at which dextrose can be infused without producing glycosuria is 0.5 g/kg/hour; at a rate of 0.8 g/kg/hour, about 95% of the infused dextrose is retained. Administration of exogenous insulin may be required in order to control hyperglycemia and glycosuria which may occur upon infusion of concentrated glucose solutions. When concentrated dextrose infusion is abruptly interrupted rebound hypoglycemia may occur, which can be prevented by the administration of 5% or 10% dextrose solutions. Part of the caloric requirements may be met by the infusion of I.V. fat emulsions.

Aminosyn® II 3.5% M and 4.25% M
in Dextrose Injection

SERUM ELECTROLYTES SHOULD BE MONITORED AS INDICATED. Electrolytes may be added to the nutrient solution as indicated by the patient's clinical condition and laboratory determinations of plasma values. Major electrolytes are sodium, chloride, potassium, phosphorus, magnesium and calcium. With the exception of calcium, all of the aforementioned electrolytes are contained in the Aminosyn II 3.5% M or 4.25% M. A calcium supplement is recommended for central vein nutritional admixtures. Alternate electrolyte additives may be used at the clinician's discretion.

Vitamins, including folic acid and vitamin K are required additives. The trace element supplements should be given when long-term parenteral nutrition is undertaken.

Iron is added to the solution or given intramuscularly in depot form as indicated. Vitamin B_{12}, vitamin K and folic acid are given intramuscularly or added to the solution as desired.

In patients with hyperchloremic or other metabolic acidosis, sodium and potassium may be added as the acetate or lactate salts to provide bicarbonate alternates.

In adults, hypertonic mixtures of amino acids and dextrose may be safely administered by continuous infusion through a central venous catheter with the tip located in the vena cava.

Pediatric

Due to their concentration, these solutions are not recommended for use in pediatric patients less than 1 year old. Pediatric requirements for parenteral nutrition are constrained by the greater relative fluid requirements of the infant and greater caloric requirements per kilogram. Pediatric patients greater than 1 year old generally receive a 2 to 2.5% amino acid solution, but older pediatric patients can tolerate amino acids in concentrations of up to 5%. Dosage is usually prescribed on a g/kg body weight/day basis and patient age as follows: ages 1 to 3 years, 2 to 2.5 g/kg/day; ages 4 to 12 years, 2 g/kg/day; ages 13 to 15 years, 1.7 g/kg/day; ages 16 and above 1.5 g/kg/day. Energy requirements for children between 1 and 7 years of age are approximately 75 to 90 kcal/kg/day; for children 7 to 12 years of age, 60 to 75 kcal/kg/day; and for ages 12 to 18 years, 30 to 60 kcal/kg/day. Energy intake may be supplemented with intravenous fat emulsion. In cases of malnutrition or stress, these requirements may be increased.

Supplemental electrolytes and vitamin additives should be administered as deemed necessary by careful monitoring of blood chemistries and nutritional status. Iron supplementation is more critical in the child than the adult because of the increasing red cell mass required by the growing child. Serum lipids should be monitored for evidence of essential fatty acid deficiency in patients maintained on fat-free TPN. Bicarbonate should not be administered during infusion of the nutritional solution unless deemed absolutely necessary.

To ensure the precise delivery of the small volumes of fluid necessary for total parenteral nutrition in children, accurately calibrated and reliable infusion systems should be used.

Drug Interactions

Additives may be incompatible. Consult with pharmacist, if available. When introducing additives, use aseptic technique, mix thoroughly and do not store.

INSTRUCTIONS FOR USE

DO NOT USE IF AMINOSYN II IS DISCOLORED OR IF CLAMP IS OPEN OR MISSING. COLOR VARIATION IN THE DEXTROSE INJECTION FROM PALE YELLOW TO YELLOW IS NORMAL AND DOES NOT ALTER EFFICACY.

To Open:

Tear outer wrap at notch. After removing the overwrap, check for minute leaks by squeezing the container firmly. If leaks are found, discard solution as sterility may be impaired. If supplemental medication is desired, follow directions below before preparing for administration.

Aminosyn® II 3.5% M and 4.25% M
in Dextrose Injection

To Add Medication:
Additives may be incompatible. See DOSAGE AND ADMINISTRATION.

1. Prepare the appropriate additive port.
2. Using aseptic technique and an additive delivery needle of appropriate length, puncture resealable additive port at target area through inner diaphragm and inject. Withdraw needle after injecting medication.
3. The additive ports should be protected by covering with additive caps.
4. Mix container contents thoroughly.

Preparation for Administration
(Use aseptic technique)

1. Open clamp between the two chambers. Completely drain all the solution and air into the lower chamber. To achieve this, stretch the side wall of the emptied top chamber. Close clamp after draining.
2. Close flow control clamp of administration set.
3. Remove cover from outlet port at bottom of container.
4. Insert piercing pin of administration set into port with a twisting motion until the set is firmly seated. **NOTE:** See full directions on administration set carton.
5. Suspend from hanger at top of container.
6. Squeeze and release drip chamber to establish proper fluid level in chamber.
7. Open flow control clamp to expel air from set. Close flow control clamp.
8. Connect to central infusion catheter.
9. Regulate rate of administration with flow control clamp. Ensure that all solution and air are in the lower chamber when reading fluid levels.

WARNING: Do not use flexible container in series connections.

HOW SUPPLIED
The Nutrimix® dual-chamber flexible container provides 500 mL of Aminosyn II 3.5% M or 4.25% M in the upper chamber and 500 mL of Dextrose Injection, USP in the lower chamber. Concentrations provided in the separate chambers and in the combined 1000 mL volume after release of the clamp and mixing are shown below.

	Concentrations Prior to Admixture		Concentrations Following Admixture		
List No.	Aminosyn II	Dextrose	Aminosyn II	Dextrose	Total Admixture Volume
7740	7% M*	10%	3.5% M*	5%	1000 mL
7742	8.5% M*	20%	4.25% M*	10%	1000 mL

*Contains maintenance electrolytes.

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (25°C); however, brief exposure up to 40° C does not adversely affect the product.

Avoid exposure to light.

Revised: May, 2004

Hospira

Hospira, Inc., Lake Forest, IL 60045 USA Reference EN-0130

Aminosyn® II 8.5% WITH ELECTROLYTES
Sulfite-Free

℞ only

AN AMINO ACID INJECTION WITH ELECTROLYTES
Flexible Plastic Container

DESCRIPTION
Aminosyn® II 8.5% WITH ELECTROLYTES, Sulfite-Free, (an amino acid injection with electrolytes) is a sterile, nonpyrogenic solution for intravenous infusion. Aminosyn II 8.5% WITH ELECTROLYTES is oxygen sensitive. The following formulation is available:

Essential Amino Acids (mg/100 mL)	
Isoleucine	561
Leucine	850
Lysine (acetate)*	893
Methionine	146
Phenylalanine	253
Threonine	340
Tryptophan	170
Valine	425

*Amount cited is for lysine alone and does not include the acetate salt.

Nonessential Amino Acids (mg/100 mL)	
Alanine	844
Arginine	865
L-Aspartic Acid	595
L-Glutamic Acid	627
Histidine	255
Proline	614
Serine	450
N-Acetyl-L-Tyrosine	230
Glycine	425

Product Characteristics	
Protein Equivalent (approx. g/liter)	85
Total Nitrogen (g/liter)	13.0
Osmolarity (mOsmol/L)	920
pH[a]	5.8
range	5.0 - 6.5

[a]Contains sodium hydroxide for pH adjustment.

Electrolytes (mEq/liter)	
Sodium (Na^+)[b]	78
Potassium (K^+)	66
Magnesium (Mg^{++})	10
Phosphorus mM[c]	30
Chloride (Cl^-)	86
Acetate ($C_2H_3O_2^-$)	61[d]

[b]Includes sodium from the pH adjustor.
[c]mM = millimoles; one mM of phosphorus = 31 mg P.
[d]Includes acetate from lysine acetate.

Hospira, Inc., Lake Forest, IL 60045 USA Reference EN-0546

Aminosyn® II 8.5% WITH ELECTROLYTES
Sulfite-Free

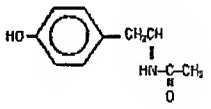
Electrolytes (mg/100 mL)	
Sodium Chloride[e]	60 mg
Magnesium Chloride hexahydrate[f]	102 mg
Sodium Phosphate, dibasic[g]	425 mg
Potassium Chloride[h]	492 mg

[e] Sodium Chloride, USP is chemically designated NaCl, a white crystalline powder freely soluble in water.
[f] Magnesium Chloride, USP is chemically designated magnesium chloride, hexahydrate, $MgCl_2 \cdot 6H_2O$, deliquescent crystals very soluble in water.
[g] Sodium Phosphate, dibasic, USP is chemically designated Na_2HPO_4, white granules very soluble in water.
[h] Potassium Chloride, USP is chemically designated KCl, a white granular powder freely soluble in water.

The formulas for the individual amino acids present in Aminosyn II 8.5% WITH ELECTROLYTES are as follows:

Essential Amino Acids	
Isoleucine, USP	$C_6H_{13}NO_2$
Leucine, USP	$C_6H_{13}NO_2$
Lysine Acetate, USP	$C_6H_{14}N_2O_2 \cdot CH_3COOH$
Methionine, USP	$C_5H_{11}NO_2S$
Phenylalanine, USP	$C_9H_{11}NO_2$
Threonine, USP	$C_4H_9NO_3$
Tryptophan, USP	$C_{11}H_{12}N_2O_2$
Valine, USP	$C_5H_{11}NO_2$

Nonessential Amino Acids	
Alanine, USP	$C_3H_7NO_2$
Arginine, USP	$C_6H_{14}N_4O_2$
L-Aspartic Acid	$C_4H_7NO_4$ $HO_2CCH_2CH(NH_2)CO_2H$
L-Glutamic Acid	$C_5H_9NO_4$ $HO_2CCH_2CH_2CH(NH_2)CO_2H$
Glycine, USP	$C_2H_5NO_2$
Histidine, USP	$C_6H_9N_3O_2$
Proline, USP	$C_5H_9NO_2$
Serine, USP	$C_3H_7NO_3$
N-Acetyl-L-Tyrosine	$C_{11}H_{13}NO_4$



The flexible plastic container is fabricated from a specially formulated polyvinylchloride. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly.

Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials.

Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

Aminosyn® II 8.5% WITH ELECTROLYTES
Sulfite-Free

CLINICAL PHARMACOLOGY

Aminosyn II 8.5% WITH ELECTROLYTES, Sulfite-Free, (an amino acid injection with electrolytes) provides crystalline amino acids to promote protein synthesis and wound healing, and to reduce the rate of endogenous protein catabolism. Aminosyn II 8.5% WITH ELECTROLYTES, given by central venous infusion in combination with concentrated dextrose, electrolytes, vitamins, trace metals, and ancillary fat supplements, constitutes total parenteral nutrition (TPN). Aminosyn II 8.5% WITH ELECTROLYTES can also be administered by peripheral vein with dextrose and maintenance electrolytes. Intravenous fat emulsion may be substituted for part of the carbohydrate calories during either TPN or peripheral vein administration of Aminosyn II 8.5% WITH ELECTROLYTES.

INDICATIONS AND USAGE

Aminosyn II 8.5% WITH ELECTROLYTES, Sulfite-Free, (an amino acid injection) infused with dextrose by peripheral vein infusion is indicated as a source of nitrogen in the nutritional support of patients in whom, for short periods of time, oral nutrition cannot be tolerated, is undesirable, or inadequate.

Aminosyn II 8.5% WITH ELECTROLYTES can be administered peripherally with dilute (5 to 10%) dextrose solution and I.V. fat emulsion as a source of nutritional support. This form of nutritional support can help to preserve protein and reduce catabolism in stress conditions where oral intake is inadequate.

When administered with concentrated dextrose solution with or without fat emulsions, Aminosyn II 8.5% WITH ELECTROLYTES is also indicated for central vein infusion to prevent or reverse negative nitrogen balance in patients where: (a) the alimentary tract, by the oral, gastrostomy or jejunostomy route cannot or should not be used; (b) gastrointestinal absorption of protein is impaired; (c) metabolic requirements for protein are substantially increased as with extensive burns and (d) morbidity and mortality may be reduced by replacing amino acids lost from tissue breakdown, thereby preserving tissue reserves, as in acute renal failure.

CONTRAINDICATIONS

This preparation should not be used in patients with hepatic coma or metabolic disorders involving impaired nitrogen utilization.

WARNINGS

Intravenous infusion of amino acids may induce a rise in blood urea nitrogen (BUN), especially in patients with impaired hepatic or renal function. Appropriate laboratory tests should be performed periodically and infusion discontinued if BUN levels exceed normal postprandial limits and continue to rise. It should be noted that a modest rise in BUN normally occurs as a result of increased protein intake.

Administration of amino acid solutions to a patient with hepatic insufficiency may result in serum amino acid imbalances, metabolic alkalosis, prerenal azotemia, hyperammonemia, stupor and coma.

Administration of amino acid solutions in the presence of impaired renal function may augment an increasing BUN, as does any protein dietary component.

Solutions containing sodium ion should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency and in clinical states in which there exists edema with sodium retention.

Solutions which contain potassium ion should be used with great care, if at all, in patients with hyperkalemia, severe renal failure and in conditions in which potassium retention is present.

Solutions containing acetate ion should be used with great care in patients with metabolic or respiratory alkalosis. Acetate should be administered with great care in those conditions in which there is an increased level or an impaired utilization of this ion, such as severe hepatic insufficiency.

Aminosyn II 8.5% WITH ELECTROLYTES, Sulfite-Free, (an amino acid injection) may not be suitable for use in infants who require individualized electrolyte therapy.

Hyperammonemia is of special significance in infants, as it can result in mental retardation. Therefore,

it is essential that blood ammonia levels be measured frequently in infants.

Instances of asymptomatic hyperammonemia have been reported in patients without overt liver dysfunction. The mechanisms of this reaction are not clearly defined, but may involve genetic defects and immature or subclinically impaired liver function.

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

Special care must be taken when administering glucose to provide calories in diabetic or prediabetic patients.

Feeding regimens which include amino acids should be used with caution in patients with history of renal disease, pulmonary disease, or with cardiac insufficiency so as to avoid excessive fluid accumulation.

The effect of infusion of amino acids, without dextrose, upon carbohydrate metabolism of children is not known at this time.

Nitrogen intake should be carefully monitored in patients with impaired renal function.

For long-term total nutrition, or if a patient has inadequate fat stores, it is essential to provide adequate exogenous calories concurrently with the amino acids. Concentrated dextrose solutions are an effective source of such calories. Such strongly hypertonic nutrient solutions should be administered through an indwelling intravenous catheter with the tip located in the superior vena cava.

SPECIAL PRECAUTIONS FOR CENTRAL VENOUS INFUSIONS

ADMINISTRATION BY CENTRAL VENOUS CATHETER SHOULD BE USED ONLY BY THOSE FAMILIAR WITH THIS TECHNIQUE AND ITS COMPLICATIONS.

Central vein infusion (with added concentrated carbohydrate solutions) of amino acid solutions requires a knowledge of nutrition as well as clinical expertise in recognition and treatment of complications. Attention must be given to solution preparation, administration and patient monitoring. IT IS ESSENTIAL THAT A CAREFULLY PREPARED PROTOCOL BASED ON CURRENT MEDICAL PRACTICES BE FOLLOWED, PREFERABLY BY AN EXPERIENCED TEAM.

SUMMARY HIGHLIGHTS OF COMPLICATIONS (consult current medical literature).

1. **Technical**
   The placement of a central venous catheter should be regarded as a surgical procedure. One should be fully acquainted with various techniques of catheter insertion. For details of technique and placement sites, consult the medical literature. X-ray is the best means of verifying catheter placement. Complications known to occur from the placement of central venous catheters are pneumothorax, hemothorax, hydrothorax, artery puncture and transection, injury to the brachial plexus, malposition of the catheter, formation of arteriovenous fistula, phlebitis, thrombosis and air and catheter emboli.
2. **Septic**
   The constant risk of sepsis is present during administration of total parenteral nutrition. It is imperative that the preparation of the solution and the placement and care of catheters be accomplished under strict aseptic conditions.

   Solutions should ideally be prepared in the hospital pharmacy under a laminar flow hood using

careful aseptic technique to avoid inadvertent touch contamination. Solutions should be used promptly after mixing. Storage should be under refrigeration and limited to a brief period of time, preferably less than 24 hours.

Administration time for a single container and set should never exceed 24 hours.

3. **Metabolic**

The following metabolic complications have been reported with TPN administration: metabolic acidosis and alkalosis, hypophosphatemia, hypocalcemia, osteoporosis, hyperglycemia, hyperosmolar nonketotic states and dehydration, glycosuria, rebound hypoglycemia, osmotic diuresis and dehydration, elevated liver enzymes, hypo- and hypervitaminosis, electrolyte imbalances and hyperammonemia in children. Frequent evaluations are necessary especially during the first few days of therapy to prevent or minimize these complications.

Administration of glucose at a rate exceeding the patient's utilization rate may lead to hyperglycemia, coma and death.

Pregnancy Category C

Animal reproduction studies have not been conducted with Aminosyn II 8.5% WITH ELECTROLYTES, Sulfite-Free, (an amino acid injection). It is not known whether Aminosyn II 8.5% WITH ELECTROLYTES can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Aminosyn II 8.5% WITH ELECTROLYTES should be given to a pregnant woman only if clearly needed.

Geriatric Use

Clinical studies of Aminosyn II 8.5% WITH ELECTROLYTES have not been performed to determine whether patients over 65 years respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for elderly patients should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal functions.

CLINICAL EVALUATION AND LABORATORY DETERMINATIONS, AT THE DISCRETION OF THE ATTENDING PHYSICIAN, ARE NECESSARY FOR PROPER MONITORING DURING ADMINISTRATION. Do not withdraw venous blood for blood chemistries through the peripheral infusion site, as interference with estimations of nitrogen containing substances may occur. Blood studies should include glucose, urea nitrogen, serum electrolytes, ammonia, cholesterol, acid-base balance, serum proteins, kidney and liver function tests, osmolarity and hemogram. White blood count and blood cultures are to be determined if indicated. Urinary osmolality and glucose should be determined as necessary.

Aminosyn II 8.5% WITH ELECTROLYTES contains no more than 25 mcg/L of aluminum.

Drug Interactions

Because of its antianabolic activity, concurrent administration of tetracycline may reduce the potential anabolic effects of amino acids infused with dextrose as part of a parenteral feeding regimen.

Additives may be incompatible. Consult with pharmacist if available. When introducing additives, use aseptic technique, mix thoroughly and do not store.

ADVERSE REACTIONS

Peripheral Infusions

A 3.5% to 5% solution of amino acids (without additives) is slightly hypertonic. Local reactions consisting of a warm sensation, erythema, phlebitis and thrombosis at the infusion site have occurred with peripheral intravenous infusion of amino acids particularly if other substances, such as antibiotics, are also administered through the same site. In such cases the infusion site should be changed promptly to another

vein. Use of large peripheral veins, inline filters, and slowing the rate of infusion may reduce the incidence of local venous irritation. Electrolyte additives should be spread throughout the day. Irritating additive medications may need to be infused at another venous site.

Generalized flushing, fever and nausea also have been reported during peripheral infusions of amino acid solutions.

OVERDOSAGE

In the event of overhydration or solute overload, re-evaluate the patient and institute appropriate corrective measures. See WARNINGS and PRECAUTIONS.

DOSAGE AND ADMINISTRATION

The total daily dose of the solution depends on the daily protein requirements and on the patient's metabolic and clinical response. In many patients, provision of adequate calories in the form of hypertonic dextrose may require the administration of exogenous insulin to prevent hyperglycemia and glycosuria. To prevent rebound hypoglycemia, a solution containing 5% dextrose should be administered when hypertonic dextrose infusions are abruptly discontinued.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Central Vein Total Parenteral Nutrition

For central vein infusion with concentrated dextrose solution, alone or with I.V. lipid, the total daily dose of the amino acid solution depends upon daily protein requirements and the patient's metabolic and clinical response. The determination of nitrogen balance and accurate daily body weights, corrected for fluid balance, are probably the best means of assessing individual protein requirements.

Adults

Admixtures of 3.5 to 4.25% amino acids with 5 to 10% dextrose may be infused with a fat emulsion by peripheral vein to provide approximately 1400 to 2000 kcal/day. Fat emulsion administration should be considered when prolonged parenteral nutrition is required in order to prevent essential fatty acid deficiency (E.F.A.D.). Serum lipids should be monitored for evidence of E.F.A.D. in patients maintained on fat-free TPN.

Aminosyn II 8.5% WITH ELECTROLYTES, Sulfite-Free, (an amino acid injection) should only be infused via a central vein when admixed with sufficient dextrose to provide full caloric requirements in patients who require prolonged total parenteral nutrition. I.V. lipid may be administered to provide part of the calories, if desired. Serum lipids should be monitored for evidence of essential fatty acid deficiency in patients maintained on fat-free TPN.

Total parenteral nutrition (TPN) may be started with 10% dextrose added to the calculated daily requirement of amino acids (1.5 g/kg for a metabolically stable patient). Dextrose content is gradually increased over the next few days to the estimated daily caloric need as the patient adapts to the increasing amounts of dextrose. Each gram of dextrose provides approximately 3.4 kcal. Each gram of fat provides 9 kcal.

The average depleted major surgical patient with complications requires between 2500 and 4000 kcal and between 12 and 24 grams of nitrogen per day. An adult patient in an acceptable weight range with restricted activity who is not hypermetabolic, requires about 30 kcal/kg of body weight/day. Average daily adult fluid requirements are between 2500 and 3000 mL and may be much higher with losses from fistula drainage or in severe burns. Typically, a hospitalized patient may lose 12 to 18 grams of nitrogen a day, and in severe trauma the daily loss may be 20 to 25 grams or more.

Aminosyn II 8.5% WITH ELECTROLYTES is designed to supply necessary electrolytes to patients in a stable metabolic state (about three-fourths of all patients on total parenteral nutrition). Other patients may require more or less of the electrolytes present, e.g., cardiac patients who should not receive sodium.

Aminosyn® II 8.5% WITH ELECTROLYTES
Sulfite-Free

Aminosyn II 8.5% WITH ELECTROLYTES does not contain calcium, and this should be added as indicated.

SERUM ELECTROLYTES SHOULD BE MONITORED AS INDICATED. Electrolytes may be added to the nutrient solution as indicated by the patient's clinical condition and laboratory determinations of plasma values. Major electrolytes are sodium, chloride, potassium, phosphate, magnesium and calcium. Vitamins, including folic acid and vitamin K are required additives. The trace element supplements should be given when long-term parenteral nutrition is undertaken.

Calcium and phosphorus are added to the solution as indicated. The usual dose of phosphorus added to a liter of TPN solution (containing 25% dextrose) is 12 mM. This requirement is related to the carbohydrate calories delivered. Iron is added to the solution or given intramuscularly in depot form as indicated. Vitamin B_{12}, vitamin K and folic acid are given intramuscularly or added to the solution as desired.

Calcium and phosphorus additives are potentially incompatible when added to the TPN admixture. However, if one additive is added to the amino acid container, and the other to the container of concentrated dextrose, and if the contents of both containers are swirled before they are combined, then the likelihood of physical incompatibility is reduced.

In patients with hyperchloremic or other metabolic acidosis, sodium and potassium may be added as the acetate or lactate salts to provide bicarbonate alternates.

In adults, hypertonic mixtures of amino acids and dextrose may be safely administered by continuous infusion through a central venous catheter with the tip located in the vena cava. Typically, the 8.5% solution is used in equal volume with 50% or 70% dextrose to provide an admixture containing 4.25% amino acids and 25% or 35% dextrose respectively.

The rate of intravenous infusion initially should be 2 mL/min and may be increased gradually. If administration should fall behind schedule, no attempt to "catch up" to planned intake should be made. In addition to meeting protein needs, the rate of administration is governed by the patient's glucose tolerance estimated by glucose levels in blood and urine.

Aminosyn II 8.5% WITH ELECTROLYTES solution, when mixed with an appropriate volume of concentrated dextrose, offers a higher concentration of calories and nitrogen per unit volume. This solution is indicated for patients requiring larger amounts of nitrogen than could otherwise be provided or where total fluid load must be kept to a minimum, for example, patients with renal failure.

Provision of adequate calories in the form of hypertonic dextrose may require exogenous insulin to prevent hyperglycemia and glycosuria. To prevent rebound hypoglycemia, do not abruptly discontinue administration of nutritional solutions.

Pediatric

Aminosyn II 8.5% WITH ELECTROLYTES may not be suitable for use in infants whose electrolyte requirements must be "custom tailored" based on serial blood chemistry determinations.

Pediatric requirements for parenteral nutrition are constrained by the greater relative fluid requirements of the infant and greater caloric requirements per kilogram. Amino acids are probably best administered in a 2.5% concentration. For most pediatric patients on intravenous nutrition, 2.5 grams amino acids/kg/day with dextrose alone or with I.V. lipid calories of 100 to 130 kcal/kg/day is recommended. In cases of malnutrition or stress, these requirements may be increased. It is acceptable in pediatrics to start with a nutritional solution of half strength at a rate of about 60 to 70 mL/kg/day. Within 24 to 48 hours the volume and concentration of the solution can be increased until the full strength pediatric solution (amino acids and dextrose) is given at a rate of 125 to 150 mL/kg/day.

Supplemental electrolytes and vitamin additives should be administered as deemed necessary by careful monitoring of blood chemistries and nutritional status. Addition of iron is more critical in the infant than the adult because of the increasing red cell mass required for the growing infant. Serum lipids should be monitored for evidence of essential fatty acid deficiency in patients maintained on fat-free TPN. Bicarbonate should not be administered during infusion of the nutritional solution unless deemed absolutely necessary.

Aminosyn® II 8.5% WITH ELECTROLYTES
Sulfite-Free

To ensure the precise delivery of the small volumes of fluid necessary for total parenteral nutrition in infants, accurately calibrated and reliable infusion systems should be used.

A basic solution for pediatric use should contain 25 grams of amino acids and 200 to 250 grams of glucose per 1000 mL, administered from containers containing 250 or 500 mL. Such a solution given at the rate of 145 mL/kg/day provides 130 kcal/kg/day.

WARNING: Do not use flexible container in series connections.

HOW SUPPLIED

List No.	Concentration	Container (mL)
4171	Aminosyn II 8.5% WITH ELECTROLYTES, Sulfite-Free, (an amino acid injection)	500

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.] **Avoid exposure to light.**

Revised: November, 2004

Hospira

Hospira, Inc., Lake Forest, IL 60045 USA
Reference EN-0546